

## REMARKS

### 1. Preliminary Remarks

Claims 18-29 are pending and under active consideration. Applicant respectfully requests that entry of the remarks made herein into the file history of this application.

### 2. Patentability Remarks

#### a. 35 U.S.C. §101

On pages 2-6 of the Office Action, the Examiner maintained the rejection of claims 18-29 under 35 U.S.C. §101 as allegedly lacking specific, substantial or credible utility. The Applicant respectfully traverses.

Specifically, the Applicant asserts that the Examiner has impermissibly applied a higher evidentiary standard for establishing utility of the claimed nucleic acids. Any utility inquiry must start by asking if there is any reason to question the truth of the statement of utility. This can be done by simply evaluating the logic of the statements made and taking into consideration any evidence cited by the Applicant as compliance with 35 U.S.C §101 is a question of fact. *See Raytheon v. Roper* 724 F.2d 951 (Fed. Cir. 1983). The evidentiary standard that the Patent Office **should** use throughout *ex parte* examination in setting forth the utility rejection is preponderance of the totality of the evidence under consideration. A preponderance of the evidence exists when it suggests that it is more likely than not that the assertion is true. *See Herman v. Huddleston*, 459 U.S. 375 (1983).

To overcome the presumption of truth of the Applicant's assertion of utility, the Examiner must establish by presenting countervailing facts that it is more likely than not that one of ordinary skill in the art would doubt (or question) the truth of the statement of utility. The crux of the Examiner's rejection is that Applicant's assertion that the claimed miR nucleic acids do bind and inhibit expression of SRY mRNA transcripts lacks credibility. The Examiner asserts that the prediction model taught by the Applicant provides no evidence that the claimed nucleic acids function as miRNA-like molecules. The Examiner presents the alleged countervailing facts that at the time of filing, prediction of miRNAs yielded predictions that were not valid citing John *et al.*, *PLoS Biology* 2:1862-1879 (2004)(hereafter "John"), and points to page 1865 in John that states that the "percentage of false positives for target transcripts with more than two, three, and four sites is 39%, 30%, and 24% respectively" and "false positive rates for single sites is about 35%". Moreover, the Examiner repeatedly states that the function of SEQ ID NO: 8385 as a functional miRNA that targets and modulates expression of SRY must be shown experimentally. In other words, the Examiner requires experimental certainty or 100% assurance that the claimed nucleic acids act or form a miRNA in order to remove any question of truth to the stated utility. Applicant submits this application of the law is impermissible.

Applicant submits that an assertion is credible unless (A) the logic underlying the assumption is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. For example, as discussed in §2107.02 III B of the MPEP, an assertion of utility would not be considered credible where a person of ordinary skill would consider the assertion to be “incredible in view of contemporary knowledge” and where nothing offered by the Applicant would counter what contemporary knowledge might otherwise suggest. Rejections under 35 U.S.C. §101 based on lack of credible utility have been sustained by federal courts when the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it **violated a scientific principle or was wholly inconsistent with contemporary knowledge in the art.** See *In re Gazave*, 379 F.2d 973 (CCPA 1967).

In response to the Examiner’s assertions and the stated law above, the Applicant reasserts that Dr. Pilpel’s Declaration (“Declaration”) filed May 27, 2008 established that the claimed nucleic acids would likely inhibit expression of SRY mRNA transcripts based upon the microRNA:target mRNA binding characteristics (see paragraphs 2 and 3 of the Declaration). Table A of the Declaration shows that the algorithm Target Scan also predicted the claimed miRNA (SEQ ID NO: 8385) binding the target mRNA (SRY). As discussed in the Declaration, the TargetScan algorithm developed by Lewis *et al*, *Cell* 115:787-798 (2003) successfully predicted miRNA/target binding between 69-78% of the time. These statements and facts would not be considered by a person of ordinary to be “incredible in view of contemporary knowledge. Even the Examiner acknowledges throughout the rejection that the miRNA/target prediction algorithms in the art such as TargetScan or John have a false positive rate for a single site between 22-35% (and therefore a success rate of 69-78% certainty).

In summary, the Examiner impermissibly requires that Applicant provide absolute certainty (100%) that SEQ ID NO: 8385 functions as a miRNA and targets/modulates SRY. Unlike the facts in *Gazave*, the Examiner’s rejection for lack of credible utility is maintained despite the fact that Dr. Pilpel’s declaration states that Applicant’s algorithm does not violate any scientific principle and is wholly consistent with contemporary knowledge regarding miRNA prediction algorithms like Target Scan and the Examiner’s cited algorithm from John. The algorithms acknowledged by the Examiner predict miRNA/target binding predict at a 69-78% success rate. The Examiner has also provided no evidence to countervail Dr. Pilpel’s statements that the microRNA SEQ ID NO: 8385 is likely to inhibit expression of the SRY protein. The Applicant submits that the Examiner has failed to present the required countervailing facts that it is more likely than not that one of ordinary skill in the art would doubt (or question) the truth of the statement of utility. In other words, the Examiner has failed to provide greater than 50% assurance that one of ordinary skill in the art would doubt (or question) the truth of the

statement of utility. Accordingly, the Examiner has failed to provide by a preponderance of the evidence that Applicant's asserted utility fails.

With regard to the Examiner's rejection regarding specific and substantial utility, the Examiner has not provided any further comment than those made in the previous office action dated November 28, 2007. Applicant reasserts that the claimed nucleic acids are of a specific and unique nature because these nucleic acids regulate the translation of mRNAs from the specific target gene SRY. Applicant also presents again the fact that study of the regulation of SRY is a public benefit one reason which is the ability of the claimed nucleic acids to modulate the expression of the SRY in order to affect gonadal hormone levels and male development. Accordingly, Applicant asserts that the claimed nucleic acids have specific, substantial and credible utility. In view of the foregoing, Applicant requests that the rejection of claims 18-29 under 35 U.S.C. §101 for lacking utility has been overcome and therefore should be withdrawn.

**b. 35 U.S.C. §112, First Paragraph (Enablement)**

On page 7 of the Office Action, the Examiner maintained the rejection of claims 18-29 under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the enablement requirement. The Examiner asserts that there is no support in the instant application for the claimed nucleic acids functioning as miRNAs, and that the claimed nucleic acids lack utility. Applicant respectfully disagrees.

As discussed above, the claimed nucleic acids have a credible, substantial and specific utility, namely in modulating expression of the SRY transcript, which in turn, may respectfully alter gonadal hormone levels and male development. Moreover, Table 7, lines 1900809-1900813 and Table 8, lines 490350-4903970 of the application first disclosed this asserted utility of the claimed nucleic acids to inhibit SRY. Therefore, the Applicant submits that the function of the claimed nucleic acids was known at the time of filing. In view of the foregoing remarks Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 18-29 under 35 U.S.C. §112, first paragraph.

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification of to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

POLSINELLI SHUGHART PC

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On behalf of: Teddy C. Scott, Jr., Ph.D.  
Registration No. 53,573

By: /Paul A. Jenny/  
Paul A. Jenny  
Registration No. 59014  
Customer No. 37808

POLSINELLI SHUGHART PC  
180 N. Stetson Ave., Suite 4525  
Chicago, IL 60601  
312.819.1900 (main)  
312.602.3955 (E-fax)  
312.873.3613 (direct)